UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
NATIONAL HEALTH AND ENVIRONMENTAL EFFECTS
RESEARCH LABORATORY
RESEARCH TRIANGLE PARK, NC 27711

CROFTON, 1998c

OFFICE OF
RESEARCH AND DEVELOPMENT

MEMORANDUM

Date: 29 December 1998

Subject: Preliminary Analysis of the Postnatal Day 12 Neuromorphology Data from the Rat Developmental Neurotoxicology Study

From: Kevin M. Crofton
Neurotoxicology Division, MD-74B
National Health Effects and Environmental Research Laboratory

To: Annie Jarabek
National Center for Environmental Assessment

This memo contains my preliminary report on the PND12 neuromorphology data. Due to the late arrival of the final report on the requested "next lower dosage" analysis and the need to keypunch all the data only a preliminary reanalysis has been done. I will attempt to have a final analysis of all the data available for the external peer review.

All data analyzed herein is contained in York (1998d) and Argus (1998a, Appendix P).

Due to time constraints the preliminary reanalysis of the control, 3 and 10 mg/kg/day groups (York 1998d) was restricted to the corpus callosum because this was the area with the largest effect. The analysis revealed no interaction of gender and treatment, however, there was a significant effect of treatment [$F(2,30)=7.65$, $p<0.0021$]. Mean contrast tests revealed a significant increase in the size of the corpus callosum only in 10 mg/kg/day group. Group means were 288, 278 and 366, for the control 3 and 10 mg/kg/day groups, respectively. Incorporation of historical control data from both PND10 and 12 (mean for controls = 264 for PND10 and 265 for PND12; York, 1998a) supports the conclusion that the control values for corpus callosum size in the York (1998a) (see also Argus, 1998a) data set are within 'normal' range. EPA does not agree with the argument put forth in Argus (1998a) that these effects are "not suggestive of a neurotoxic effect" due to "an unknown biological significance". EPA considers a 27% increase in the size of any brain region to be a potentially adverse effect (USEPA,1998b). Therefore, the LOAEL is 10 mg/kg/day and the NOAEL is 3 mg/kg/day.